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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,185	12/31/2003	George M. Halow	A-8636	5571

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EXAMINER	
LEWIS, AMY A	
ART UNIT	**PAPER NUMBER**
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/748,185	HALOW, GEORGE M.	
	Examiner	Art Unit	
	Amy A. Lewis	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Case

The Amendment and Remarks, filed 1 November 2005, have been entered into the application. Accordingly, claims 1, 3, 4, 7-11, and 15-25 have been amended, and claims 26-32 have been added.

Claims 1-32, as filed 1 November 2005, are presented for examination.

Response to Remarks, filed 1 November 2005:

1) Rejection of claims 15-25 under 35 U.S.C. 112, second paragraph has been withdrawn in view of amendments to the claims.

2) Rejection of claims 1 and 2 under 35 U.S.C. 102(b) as being anticipated by Roblin, et al. ("Use of polyethylene glycol 4000 in hepatic encephalopathy related to digestive hemorrages," *Gastroenterol Clin Biol* 1994 18(12): 1146) is *withdrawn* in view of the fact that the current claims are drawn to orally administered PEG.

Applicant argues that the "article describes a method for treatment of ruptured esophogael varicose veins associated with portal hypertension in a cirrhosis patient with hepatic encephalopathy (HE), comprising the administration of 2 liters of a PEG 4000 (Fortans 7) via a gastric probe..." (see p. 1, last paragraph of Remarks). And that Roblin's disclosed method is limited to the use of a gastric lavage administered through a gastric probe (tube) to evacuate intestinal blood resulting from acute and abundant digestive hemorrhage..." (see p. 2, paragraph 2 of Remarks). Applicant also states that "Roblin specifies his goal as the treatment of HE

during digestive hemorrhaging" (see p. 2, paragraph 2 of Remarks). Applicant distinguishes their claims from the Roblin art in that the claimed composition and method of treatment is oral administration of a "liquid drink" composition.

In response to Applicant's argument that "Roblin specifies his goal as the treatment of HE during digestive hemorrhaging" (see p. 2, paragraph 2 of Remarks), the current claims are directed to a method of treating HE; regardless of whether the HE is caused by digestive hemorrhaging, Roblin nonetheless teaches a method of treating HE, as is instantly claimed.

3) Rejection of claims 1, 4, 19, 22 and 23 under 35 U.S.C. 103(a) as being unpatentable over Roblin, et al. "Use of polyethylene glycol 4000 in hepatic encephalopathy related to digestive hemorrages," *Gastroenterol Clin Biol* 1994 18(12): 1146 and Vicidomini F and Labruzzo F (EP 1230918 A2), has been withdrawn in favor of the new/modified ground of rejection set forth below.

4) Rejection of claims 1-25 under 35 U.S.C. 103(a) as being unpatentable over Roblin, et al. "Use of polyethylene glycol 4000 in hepatic encephalopathy related to digestive hemorrages," *Gastroenterol Clin Biol* 1994 18(12): 1146 and Vicidomini F and Labruzzo F (EP 1230918 A2), as applied to claims 1, 4, 19, 22 and 23 above, and further in view of Pelham et al. (US 2005/0152989 A1), has been withdrawn in favor of the new/modified ground of rejection set forth below.

NEW/MODIFIED GROUNDS OF REJECTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1) Claims 1, 4, 10, 19, and 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roblin, et al. ("Use of polyethylene glycol 4000 in hepatic encephalopathy related to digestive hemorrages," *Gastroenterol Clin Biol* 1994 18(12): 1146), in view of Mosby's (Mosby's GenRx: The complete reference for generic and brand drugs, Eighth Edition, 1998, Mosby—Year Book Inc., Publishers, St. Louis, p. II-1169 & II-1770), and further in view of Vicidomini F and Labruzzo F (EP 1230918 A2).

Roblin teaches treatment of hepatic encephalopathy (HE) during digestive hemorrhaging by administration of 2 L of polyethylene glycol 4000 (Fortans 7) in two hours by Blakemore probe. The reference states that "twenty patients has this protocol

for treating hepatic encephalopathy linked to digestive hemorrhage by rupture of esophageal varicose veins". (See p. 1, paragraphs 3-4 of the translated article).

In response to Applicant's argument that "Roblin specifies his goal as the treatment of HE during digestive hemorrhaging" (see p. 2, paragraph 2 of Remarks), the current claims are directed to a method of treating HE; regardless of whether the HE is caused by digestive hemorrhaging, Roblin nonetheless teaches a method of treating HE, as is instantly claimed.

Mosby's teaches administration oral compositions of polyethylene glycol 3350. The PEG is supplied as either reconstituted powder or a solution. See: p. II-1770.

Vicidomini teaches an aqueous enteroclysis solution containing, as an active ingredient, lactulose for the treatment of hepatic encephalopathy, particularly of porto-systemic encephalopathy (abstract). The reference also teaches that among factors which promote occurrence of porto-systemic encephalopathy are metabolic alkalosis (i.e. increased levels of ammonia) and constipation ([0004]). The reference also teaches that lactulose reduces the pH in the colon and inhibits the production of ammonia ([0007]). The reference teaches that the aqueous solution contains a quantity of disaccharide (i.e. lactulose) ranging from between 0.05 g/mL to 0.5 g/mL, and that the solution is prepared by adding the components directly to spring water, both of which are in crystalline form and soluble in water (paragraphs [16-17]), thus meeting the limitations that the composition be in powder form and free of added electrolytes. The reference does not teach PEG for the treatment of hepatic encephalopathy.

The following case law is believed to be relevant to the instant claim rejections:

In re Kerkhoven (205 USPQ 1069, CCPA 1980) states that "It is *prima facia* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the same purpose: the idea of combining them flows logically from their having been individually taught in the prior art." Therefore, it would have been obvious to the skilled artisan to combine polyethylene glycol and lactulose, motivated by their having been taught by the prior art to be useful in treating hepatic encephalopathy characterized by constipation and increased levels of amonia, consonant with the reasoning of the cited case law. Further, it would have been obvious to make a formulation for oral administration, having been taught by Mosby's that it is known to administer PEG orally, and further motivated by ease of administration.

2) Claims 1-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roblin, et al. ("Use of polyethylene glycol 4000 in hepatic encephalopathy related to digestive hemorrages," *Gastroenterol Clin Biol* 1994 18(12): 1146), in view of Mosby's (Mosby's GenRx: The complete reference for generic and brand drugs, Eighth Edition, 1998, Mosby—Year Book Inc., Publishers, St. Louis, p. II-1169 & II-1770), and further in view of Vicidomini F and Labruzzo F (EP 1230918 A2) and Pelham et al. (US 2005/0152989 A1).

Roblin teaches treatment of hepatic encephalopathy (HE) during digestive hemorrhaging by administration of 2 L of polyethylene glycol 4000 (Fortans 7) in two hours by Blakemore probe. The reference states that "twenty patients has this protocol

for treating hepatic encephalopathy linked to digestive hemorrhage by rupture of esophageal varicose veins". (See p. 1, paragraphs 3-4 of the translated article).

In response to Applicant's argument that "Roblin specifies his goal as the treatment of HE during digestive hemorrhaging" (see p. 2, paragraph 2 of Remarks), the current claims are directed to a method of treating HE; regardless of whether the HE is caused by digestive hemorrhaging, Roblin nonetheless teaches a method of treating HE, as is instantly claimed.

Mosby's teaches administration oral compositions of polyethylene glycol 3350. The PEG is supplied as either reconstituted powder or a solution. See: p. II-1770.

Vicidomini teaches an aqueous enteroclysis solution containing, as an active ingredient, lactulose for the treatment of hepatic encephalopathy, particularly of porto-systemic encephalopathy (abstract). The reference also teaches that among factors which promote occurrence of porto-systemic encephalopathy are metabolic alkalosis (i.e. increased levels of ammonia) and constipation ([0004]). The reference also teaches that lactulose reduces the pH in the colon and inhibits the production of ammonia ([0007]). The reference teaches that the aqueous solution contains a quantity of disaccharide (i.e. lactulose) ranging from between 0.05 g/mL to 0.5 g/mL, and that the solution is prepared by adding the components directly to spring water, both of which are in crystalline form and soluble in water (paragraphs [16-17]), thus meeting the limitations that the composition be in powder form (of instant claims 19-21) and free of added electrolytes (of instant claims 22-25). The dosage range of between 0.05 g/mL to 0.5 g/mL translates to a dosage of between 10-100g of lactulose, thus meeting the specific limitations of

instant claims 8 and 13. The reference does not teach PEG for the treatment of hepatic encephalopathy.

Pelham et al. (US 2005/0152989) teaches a composition of laxitive and fiber for the treatment of irritable bowl syndrome, which includes constipation, containing lactulose and polyethylene glycol (PEG). See: abstract; paragraph [0004] and [0013]. The reference teaches that lactulose is a poorly absorbable disaccharide (i.e. fiber) (paragraph [0022]), and that PEG is an osmotic laxative which may be solid or liquid at room temp (see paragraphs [0023-0024]). The reference teaches dosages of PEG (see paragraph [0046 & 0048]) which overlap those of instant claims 3, 7, 9, 12, and 14. The reference also teaches laxative to fiber ratios of 3:1 to 1:3 and 1:1, which overlap those of instant claims 5, 6, 10, and 11 (see paragraph [0031]). The reference also teaches the composition be administered at a dose and frequency sufficient to reduce or eliminate the symptoms, such as constipation, and can be administered in one dose per day for tow or more doses and up to 12 weeks (see: abstract; paragraphs [0041-0042]; claims 12-14).

The following case law is believed to be relevant to the instant claim rejections:

In re Kerkhoven (205 USPQ 1069, CCPA 1980) states that "It is *prima facia* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the same purpose: the idea of combining them flows logically from their having been individually taught in the prior art." Therefore, it would have been obvious to the skilled artisan to combine polyethylene glycol and lactulose in an oral fomulation, motivated by their having been taught by the prior art to be useful in treating hepatic encephalopathy with

constipation and increased levels of amonia, and with the specific formulation and dosage ranges for a composition containing PEG and lactulose taught by Pelham et al., consonant with the reasoning of the cited case law.

Conclusion

Claims 1-32 are rejected. No claims are allowed.

Contact Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy A. Lewis whose telephone number is (571) 272-2765. The examiner can normally be reached on Monday-Friday, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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